Optimizing Diabetes care through Evidence-based Medicine and Health Economics: The German Experience

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Decision-making in the German Statutory Health Insurance

Parliament

- Legislation

Federal Ministry of Health

- Supervision

Patient

Free choice

150,000 ambulatory care physicians and psychotherapists

Federal Association of SHI Physicians (KBV)

150 sickness funds

Federal Association of Sickness Funds

Federal Joint Commitee (G-BA)

Members: 13 voting – 3 neutral + 5 sickness funds + 5 providers (+ up to 5 patient representatives)

German Hospital Federation (DKG)

2,100 hospitals

Statutory Health Insurance (85% of population covered)
Objectives of Federal Joint Committee

- Main functions: to regulate SHI-wide issues of access, benefits and quality (and not primarily of costs or expenditure).
- Normative function of the G-BA by legally binding directives ("sub-law") to guarantee equal excess to necessary and appropriate services for all SHI insured.
- Benefit-package decisions must be justified by an evidence-based process to determine whether services, pharmaceuticals or technologies are medically effective in terms of morbidity, mortality and quality of life.
- By law, evidence based assessments can only be used to select the most appropriate (efficient) service etc. from others – not to prioritize among service areas: if a costly innovation has a significant additional benefit, the sickness funds must pay for it.
**Federal Joint Committee: preparation of decisions**

Decisions are prepared by 8 sub-committees:

- Pharmaceuticals
- Quality Assurance
- Cross-sector Care (especially disease management programs)
- Methodological Evaluation (inclusion of new ambulatory care services in benefit basket; NB: in hospitals, services can only be excluded)
- Referred Services (rehabilitation, care provided by non-physicians, ambulance transportation etc.)
- Needs-based Planning (ambulatory care; NB: hospital capacities are planned by state governments)
- Psychotherapy
- Dental Services
Federal Joint Committee: support through institutes

Parliament 

Federal Ministry of Health

Legislation  

Supervision

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Statutory Health Insurance

Institute for Quality and Efficiency in Healthcare (IQWiG) – technologies

AQUA Institute for Quality – focused on providers

Federal Joint Commitee (G-BA)
Pricing and reimbursement of (new) drugs in Germany (until 2010; simplified)

Market authorization

\( t_0 \) Manufacturer sets price

\( t_0 \) Immediately prescribable (SHI covers fully)

\( t_{x1} \) Doubts about additional benefit

\( t_{x2} \)

\( t_{x3} \)

\( t_{x4} \) Additional benefit

\( t_{y1} \) Doubts about cost-effectiveness

\( t_{y2} \)

\( t_{y3} \)

\( t_{y4} \)

IQWiG evaluation: additional benefit/comparative effectiveness

IQWiG cost-effectiveness evaluation

Maximum reimbursement price
## Overview: IQWiG’s evidence reports on anti-diabetic medication

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* The Ministry of Health requested that this should not be applicable to children/adolescents under 18.
** Commissioned as a follow-up for Project “A05-02: Rapid-acting insulin analogues in the treatment of DM 1”.
A05-04: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 (I)

**Interventions assessed**
- Insulin aspart
- Insulin glulisine
- Insulin lispro

**Methods**

- **Inclusion criteria:**

| 11 | Patients with manifest diabetes mellitus type 2 as defined in Section 4.1.1. |
| 12 | Test intervention: Insulin aspart, insulin glulisine, or insulin lispro (also as premixed formulations consisting of rapid-acting insulin analogues combined with longer-acting insulins, as defined in Section 4.1.2). |
| 13 | Comparator treatment: short-acting RHI or a different insulin analogue from the group of insulin analogues mentioned above (also as premixed formulations consisting of rapid-acting insulin analogues or short-acting RHI combined with longer-acting insulins, as defined in Section 4.1.2). |
| 14 | Endpoints derived from the patient-relevant outcomes formulated in Section 4.1.3. |
| 15 | RCT (blinded or non-blinded). |
| 16 | Treatment period \( \geq 24 \) weeks (in cross-over studies: per treatment arm). |
| 17 | Language of publication: German, English, French, Dutch, Portuguese, or Spanish. |
| 18 | Location of administration: subcutaneous tissue. |
| 19 | Options for a combination with other blood glucose-lowering treatments (see also Section 4.1.2): |
|   | - No additional blood glucose-lowering treatment in either group. |
|   | - Comparable additional blood glucose-lowering treatment in both groups with drugs approved and available in Germany. |
A05-04: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 (II)

- **Patient-relevant outcomes:**
  - Reduction of total mortality;
  - Reduction of cardiac morbidity and mortality;
  - Reduction of cerebral morbidity and mortality;
  - Reduction of vascular non-cardiac and non-cerebral morbidity and mortality;
  - Reduction of the rate of blinding;
  - Reduction of the rate of terminal renal insufficiencies requiring dialysis;
  - Reduction of the rate of amputations (major and minor amputations);
  - Reduction of the hospitalisation rate (any cause);
  - Reduction of the rate of hyperglycaemic or ketoacidotic comas;
  - Reduction of the rate of symptoms caused by chronic hyperglycaemia;
  - Reduction of the rate of hypoglycaemic episodes, especially severe hypoglycaemic episodes;
  - Reduction of the rate of other adverse drug effects;
  - Preservation or improvement of disease-related QoL (including capacity to work and other activities of daily life), and treatment satisfaction.

Furthermore, HbA1c levels were recorded as a measure of the long-term lowering of blood glucose levels in order to help interpret outcomes, in particular the occurrence of hypoglycaemic episodes.
A05-04: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 (III)

Data sources

- Electronic databases: Medline, EMBASE, CENTRAL
- Reference lists of relevant HTA-reports, systematic reviews, meta-analyses
- Requests to manufacturers: Novo Nordisk Pharma GmbH, Mainz (insulin aspart), Aventis Pharma Deutschland GmbH, Bad Soden am Taunus (insulin glulisin) and Lilly Deutschland GmbH, Bad Homburg (insulin lispro)
  - Study registers
  - Websites of regulatory authorities (FDA, EMEA)
A05-04: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 (IV)

Results

- Included studies:
  - Insulin aspart: n = 0*
  - Insulin glulisin: n = 2
  - Insulin lispro: n = 5

* One study relevant for insulin aspart was not fully published; Novo Nordisk did not agree to provide data on this study given that they would be published by IQWiG as part of the assessment
A05-04: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 (V)

Conclusion

Final report A05-04: Rapid-acting insulin analogues for the treatment of diabetes mellitus type 2

8. Conclusion

For patient-relevant outcomes, there is no convincing evidence of a superiority of rapid-acting insulin analogues compared with RHI in diabetes mellitus type 2 therapy. Rapid-acting insulin analogues have not been sufficiently investigated with regard to their potential long-term beneficial and harmful effects.
Rapid-acting insulin analogues in the treatment of diabetes mellitus type 2 are excluded from prescription as long as they involve higher costs than regular human short-acting regular human insulin (with exceptional cases).
Consequences I: Changes in prescription volume

a) Prescription volume of rapid-acting insulin analogues (2004-2007)

(Source: Dorendorf & Gerhardus: Triangulation of Methods to assess the Impact of Evidence Reports. HTAi Conference 2009)
Consequences II: Rebate contracts between sickness funds and manufacturers

“AOK members still obtain short-acting insulin analogues”

“Insulin analogues still without additional costs for members of IKK Nord”

“Insulin analogues available again for statutory health insurance patients”

Insulinanologa wieder für Kassenpatienten

Novo Nordisk schließt Rabattverträge mit BEK und TK ab
Consequences III: Lawsuit against Federal Joint Committee

Lilly Deutschland and Sanofi Aventis had filed a lawsuit at the Social Court to reverse G-BA’s decision from 18.07.2006.

The lawsuit was dismissed on 15.01.2010.
### Overview: IQWiG’s evidence reports on anti-diabetic medication

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** Commissioned as a follow-up for Project “A05-02: Rapid-acting insulin analogues in the treatment of DM 1“.
A05-02: Rapid-acting insulin analogues in the treatment of DM 1
A08-01: Rapid-acting insulin analogues in children and adolescents with DM 1

06.06.2007
Final report A05-02
- Adult patients:
  “no evidence available of superiority over human insulin”
- Children and adolescents:
  “benefit in children and adolescents unclear due to lack of data;
some results from long-term comparative studies withheld by manufacturer”

16.11.2009 - A08-01
Final report on children and adolescents
“manufacturer provided additional data;
no proof of additional benefit of analogues;
insufficient research on potential harm”

21.02.2008
Decision: Exclusion from prescription, as long as higher costs involved (exceptions apply) („Verordnungseinschränkung“)

17.07.2008
Commission to IQWiG: A08-01

09.02.2010
Pending decision: Exclusion from prescription, as long as higher costs involved (exceptions apply) („Verordnungseinschränkung“) [same as before]

08.05.2008
„Beanstandung“

Exclusion from prescription is not reasonable („zumutbar“) for insured persons under 18. The decision is therefore objected („beanstandet“).
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** Commissioned as a follow-up for Project “A05-02: Rapid-acting insulin analogues in the treatment of DM 1”.
A05-05A: Glitazones in the treatment of diabetes mellitus type 2 (long-term use)

26.01.2009
Final report
- “Glitazones not sufficiently investigated,
- no long-term studies on Rosiglitazone available,
- Pioglitazone could reduce risk of later vascular complications but increase risk of heart failure”

17.06.2010
Decision: excluded from prescription without exception („Verordnungsausschluss“)

19.10.2010
Additional comment provided („ergänzende Stellungnahme“)

18.11.2010
Publication in Federal Gazette („Bundesanzeiger“)

04.08.2010
Demands further justification of the decision

03.11.2010
„Nichtbeanstandung“

01.04.2011
Decision will come into effect

Glitazones are evaluated as inexpedient as there are alternative treatments available for which a comparable potential risk is not known. G-BA places more weight on the proof of harm compared to a possible additional benefit of Glitazones.
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** The commission was awarded as a follow-up commission for Project “A05-02: Rapid-acting insulin analogues in the treatment of diabetes mellitus type 1”.
A05-05C: Glinides in the treatment of diabetes mellitus type 2 (long-term use)

04.06.2009
Final report
- “benefit of glinides not scientifically proven,
- no better performance than other antidiabetics available in tablet form,
- no proof of additional benefit”

17.06.2010 Decision:
Exclusion from prescription „Verordnungseinschränkung“

13.10.2010
Additional comment provided („ergänzende Stellungnahme“)

05.11.2010
Additional comment provided („ergänzende Stellungnahme“)

02.12.2010
Reply

01.02.2011
Reply

12.08.2010
Demands further justification of the decision

25.10.2010
Demands further justification

15.11.2010
Demands further justification

10.12.2010
Demands further justification

SGB V does not request proof of a “negative” fact; the absence of a proof of relevant effects on patient-relevant outcomes justifies the conclusion that a drug is inexpedient.

Exclusion requires proof of inexpediency („Unzweckmäßigkeit“)
Pricing and reimbursement of (new) drugs in Germany (from 2011; simplified)

**Market authorization**

- **t0** Manufacturer sets price
- **t0** Immediately prescribable (SHI covers fully)
- **t0** Dossier by manufacturer → IQWiG evaluation: additional benefit/ comparative effectiveness
- **t3**
- **t6**
- **max. t12** Negotiation manufacturer & Fed. Ass. Sickness Funds

- **Additional benefit**
- **no agreement**

- **Reference price**

**IQWiG cost-effectiveness evaluation**

Presentation available at:

www.mig.tu-berlin.de